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Facile Synthesis of Spirocyclic Ketones via Gold(I)-Catalyzed Claisen-Type Rearrangement of Cyclic 8-Aryl-2,7-enyn-1-ols

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The gold(I)-catalyzed Claisen-type rearrangement of cyclic 8-aryl-2,7-enyn-1-ols proceeds via a cationic allylic vinyl ether gold intermediate to give spirocyclic ketones. The reaction proceeded via attack of the hydroxyl group onto the gold-activated alkynes followed by [3,3]-sigmatropic rearrangement to generate the spirocyclic ketones. This transformation can be applied to the synthesis of aza- and oxaspirocyclic ketones from cyclic 8-aryl-2,7-enyn-1-ols bearing an N-sulfonamide or an oxygen atom linkage in the tether and the gold(I) catalyst.

Introduction

The construction of spirocyclic building blocks is an important synthetic goal because such ring skeletons have interesting conformational features and are present in numerous natural products of biological interest.[1] Because the availability of functionalized spirocyclic building blocks could greatly facilitate the elaboration of more complex target molecules, the design of expedient synthetic routes to such intermediates has been actively pursued.[2−7] Many synthetic methods, as the key step, have been developed in pursuit of this structure, including intramolecular alkylation,[2] radical cyclization,[3] [3,3]-sigmatropic rearrangement,[4] ring closure of geminal-disubstituted alkenes,[5] cycloaddition,[6] and transition-metal-mediated cyclization.[7] Among these, Claisen rearrangement is generally regarded as a high-performance method for diastereoselective C−C bond formation from an easily accessible C−O single bond, thereby generating two stereogenic centers and a double bond.[8] Metal-catalyzed Claisen-type rearrangement has shown significant impact due to the catalysis needing milder reaction conditions and providing better stereoselectivities compared to their thermal counterparts.[9] Recently, cationic phosphine

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(1) (a) Srivastav, N.; Mittal, A.; Kumar, A. *J. Chem. Soc., Chem. Commun.* **1992**, 493. (b) Kobayashi, J.; Tsuda, M.; Agemi, K.; Shigemiri, H.; Ishibashi, M.; Sasaki, T.; Mikami, Y. *Tetrahedron* **1991**, *47*, 6617. (c) James, D. M.; Kunze, H. B.; Faulkner, D. J. *J. Nat. Prod.* **1991**, *54*, 113. (d) Posner, G. H.; Hamill, T. G. *J. Org. Chem.* **1988**, *53*, 6031. (e) Stork, G.; Danheser, R. L.; Ganem, B. *J. Am. Chem. Soc.* **1973**, *95*, 3414. (f) Huang, H.; Forsyth, C. J. *J. Org. Chem.* **1995**, *60*, 2773. (g) Yamamoto, Y.; Furuta, T. *J. Org. Chem.* **1990**, *55*, 3971.

(2) (a) Pigge, F. C.; Coniglio, J. J.; Dalvi, R. *J. Am. Chem. Soc.* **2006**, *128*, 3498. (b) Chande, M. S.; Khanwelkar, R. R. *Tetrahedron Lett.* **2005**, *46*, 7787. (c) Kotha, S.; Manivannan, E. *Arkivoc* **2003**, 67. (d) Huang, A.; Kodanko, J. J.; Overman, L. E. *J. Am. Chem. Soc.* **2004**, *126*, 14043. (e) Bagul, T. D.; Lakshmaiah, G.; Kawabata, T.; Fuji, K. *Org. Lett.* **2002**, *4*, 249. (f) Takasu, K.; Ohsato, H.; Ihara, M. *Org. Lett.* **2003**, *5*, 3017.

(3) (a) Inui, M.; Nakazaki, A.; Kobayashi, S. *Org. Lett.* **2007**, *9*, 469. (b) Takasu, K.; Ohsato, H.; Ihara, M. *Org. Lett.* **2003**, *5*, 3017. (c) Parsons, P. J.; Caddick, S. *Tetrahedron* **1994**, *50*, 13523. (d) Ladlow, M.; Pattenden, G. *Tetrahedron Lett.* **1984**, *25*, 4317. (e) Lee, E.; Tae, J. S.; Lee, C.; Park, C. M. *Tetrahedron Lett.* **1993**, *34*, 4831.

(4) (a) Miyamoto, H.; Okawa, Y.; Nakazaki, A.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 2274. (b) Kawasaki, T.; Ogawa, A.; Terashima, R.; Saheki, T.; Ban, N.; Sekiguchi, H.; Sakaguchi, K.; Sakamoto, M. *J. Org. Chem.* **2005**, *70*, 2957. (c) Mao, Z.; Baldwin, S. W. *Org. Lett.* **2004**, *6*, 2425.

(5) (a) Fedouloff, M.; Paknoham, S. J.; Strachan, J. B.; Melville, J. L.; Voyle, M. *Tetrahedron Lett.* **2000**, *41*, 4657. (b) Somei, M.; Yamada, F.; Izumi, T.; Nakajou, M. *Heterocycles* **1997**, *45*, 2327. (c) Nakazaki, A.; Miyamoto, H.; Henmi, K.; Kobayashi, S. *Synlett* **2005**, 1417. (d) For a related example of the construction of spirocyclic compounds based on a Claisen rearrangement, see: Miyamoto, H.; Okawa, Y.; Nakazaki, A.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 2274. (e) Nakazaki, A.; Era, T.; Numada, Y.; Kobayashi, S. *Tetrahedron* **2006**, *62*, 6264.

(6) (a) Yong, S. R.; Williams, M. C.; Pyne, S. G.; Ung, A. T.; Skelton, B. W.; White, A. H.; Turner, P. *Tetrahedron* **2005**, *61*, 8120. (b) Beccalli, E. M.; Clerici, F.; Gelmi, M. L. *Tetrahedron* **2003**, *59*, 4615. (c) Okada, K.; Kondo, M.; Tanino, H.; Inoue, S. *Heterocycles* **1992**, *34*, 589. (d) Barluenga, J.; Aznar, F.; Barluenga, S.; Garcia-Granda, S.; Alvarez-Rua, C. *Synlett* **1997**, 1040. (e) Marx, J.; Norman, L. R. *J. Org. Chem.* **1975**, *40*, 1602.

(7) (a) Pearson, A. J.; Alimardonov, A.; Pinkerton, A. A.; Parrish, D. A. *J. Org. Chem.* **1998**, *63*, 6601. (b) Pearson, A. J.; Zettler, M. W. *J. Chem. Soc., Chem. Commun.* **1987**, 1243. (c) Kido, S.; Abiko, P.; Kato, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 229. (d) Cossy, J.; Bouzide, A.; Leblanc, C. *Synlett* **1993**, 202. (e) Tanaka, M.; Takahashi, M.; Sakamoto, E.; Imail, M.; Matsui, A.; Fujio, M.; Funakoshi, K.; Sakai, K.; Suemune, H. *Tetrahedron* **2001**, *57*, 1197. (f) Semmelhack, M. F.; Yamashita, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 5924. (g) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1991**, *113*, 701. (h) Villar, J. M.; Delgado, A.; Llebaria, A.; Moreto, J. M.; Molins, E.; Miravitlles, C. *Tetrahedron* **1996**, *52*, 10525. (i) Pages, L.; Llebaria, A.; Camps, F.; Molins, E.; Miravitlles, C.; Moreto, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 10449. (j) Casaschi, A.; Grigg, R.; Sansano, J. M.; Vilson, D.; Redpath, J. *Tetrahedron* **2000**, *56*, 7541.

(8) For reviews on catalysis of the Claisen rearrangement, see: (a) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205. (b) Ito, H.; Taguchi, T. *Chem. Soc. Rev.* **1999**, *28*, 43. (c) Hiersemann, M.; Abraham, L. *Eur. J. Org. Chem.* **2002**, 1461.

(9) For Lewis acid catalysis of the Claisen rearrangement see: (a) Takai, K.; Mori, I.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 3985. (b) Nonoshita, K.; Banno, H.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1990**, *112*, 316. (c) Trost, B. M.; Schroeder, G. M. *J. Am. Chem. Soc.* **2000**, *122*, 3785. (d) Hiersemann, M.; Abraham, L. *Org. Lett.* **2001**, *3*, 4952. For metal catalysis of the Claisen rearrangement see: (e) van der Baan, J. L.; Bickelhaupt, F. *Tetrahedron Lett.* **1986**, *27*, 6267. (f) Sugiura, M.; Yanagisawa, M.; Nakai, T. *Synlett* **1995**, 447. (g) Overman, L. E. *Angew. Chem., Int. Ed.* **1984**, *23*, 579.

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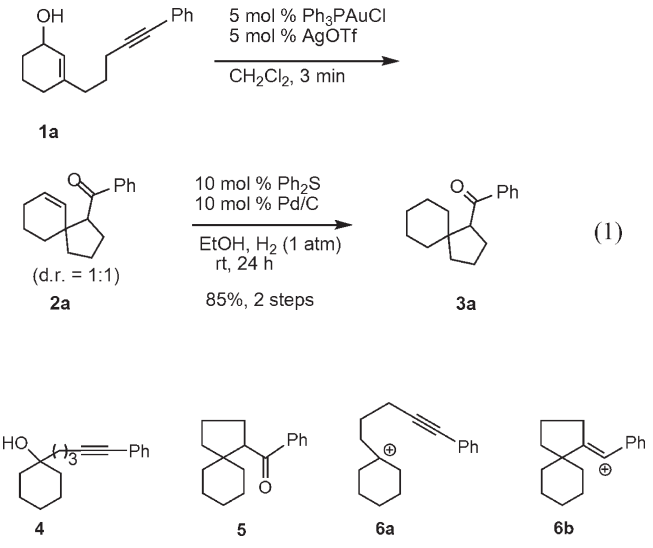
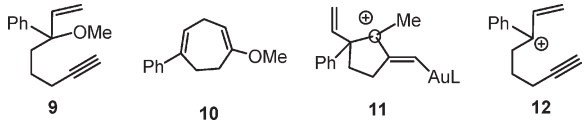
gold(I) complexes have emerged as versatile catalysts for electrophilic activation of alkynes toward a variety of nucleophiles under mild reaction conditions, allowing numerous synthetic transformations of unsaturated systems into useful structure motifs.[10] Although gold(I)-catalyzed Claisen-type rearrangement of propagylic vinyl ethers and 3-methoxy-1,6-enynes has been reported to give homoallenic alcohols[11] and cycloheptenones,[12] respectively, a general gold(I)-catalyzed Claisen-type rearrangement of cyclic 8-aryl-2,7-enyn-1-ols to give spirocycles has yet to be developed. We have now demonstrated that phosphine gold(I) can be applied toward the synthesis of spirocycles by treatment of cyclic 8-aryl-2,7-enyn-1-ols with a catalytic amount of $Ph_3PAuCl/AgOTf$. In this transformation, a nucleophilic *9-endo-dig* addition of the hydroxyl group onto the gold(I)-activated alkyne generated a cationic allylic vinyl ether gold intermediate. A subsequent Claisen-type rearrangement of the cyclic transient cationic gold intermediate produced a spirocyclic ketone. Moreover, the gold(I)-catalyzed Claisen-type rearrangement of cylic 8-aryl-2,7-enyn-1-ols containing a N-sulfonamide or an oxygen atom linkage in the tether afforded aza- and oxaspirocycles, respectively.

Results and Discussion

The requisite 8-arylcyclohex-2-en-7-yn-1-ol **1** was prepared by addition of the corresponding 5-lithio-1-arylpent-1-yne to 3-methoxycyclohex-2-en-1-one followed by reduction of the resulting enones with $NaBH_4$ in MeOH to afford 8-arylcyclohex-2-en-7-yn-1-ol **1** in good overall yields. Our study of gold(I)-catalyzed Claisen-type rearrangement of 8-arylcyclohex-2-en-7-yn-1-ols began with the parent compound **1a**. Treatment of **1a** with 5 mol % of $Ph_3PAuCl/AgOTf$ in CH_2Cl_2 at 25 °C for 3 min produced phenyl(spiro[4.5]dec-6-en-1-yl)methanone (**2a**) in 90% isolated yield as a 1:1 mixture of two diastereomers (eq 1). Attempts to separate isomers using flash column chromatography on silica gel failed. A Pd/C-catalyzed chemoselective hydrogenation of **2a** employing diphenylsulfide as a catalyst poison produced the spirocyclic ketone **3a**.[13] Thus, the crude mixture of isomer **2a**, 10 mol % Pd/C, and 10 mol % diphenylsulfide in ethanol was allowed to stir at room temperature under 1 atm of hydrogen for 24 h to provide the spirocyclic ketone **3a** in 85% isolated yield in two steps (eq 1). Decreasing the catalyst loading for the [3,3]-sigmatropic rearrangement of **1a** to 0.1 mol % slowed the reaction (90 min) but still produced **2a** in 90% yield. In contrast, when **1a** was treated with 5 mol % $PtCl_2$ in fluxing toluene, the reaction failed to give the desired spirocyclic ketone **2a**. Moreover, both Ph_3PAuCl and AgOTf are required for the rearrangement.



Recently, the Yamamoto group has reported a trifluoromethanesulfonic acid (TfOH)-catalyzed cyclization of alkynyl cyclic tertiary alcohol **4** to form the spirocyclic ketone **5** as a mixture of diastereomers in 80% yield.[14] The reaction path leading to **5** started with the formation of the tertiary carbocation (**6a**) followed by addition of the alkynyl moiety onto the cation to give a benzylidene cation (**6b**). Trapping of the reactive cation with H_2O afforded the spirocyclic ketone **5**. To investigate the possibility of an ionization pathway by the gold catalyst, the non-allylic tertiary alcohol **4** was treated with the gold(I) cation. Thus, treatment of **4** with 5 mol % of $Ph_3PAuCl/AgOTf$ in CH_2Cl_2 at 25 °C for 45 min produced cyclohexenylketone **7** in 68% isolated yield (Scheme 1). The formation of **7** may start with a 6-*exo-dig* cyclization to afford **8a** followed by proton transfer to give the cyclic vinyl ether **8b**. Deprotonation of **8b** produced the cyclohexenyl ketone **7**. On the basis of two different rearrangement products (**5** vs **7**) obtained from TfOH and the gold catalyst, it is reasonable to state that the cationic pathway suggested by Yamamoto does not apply to the gold-catalyzed transformation of **4**. Moreover, Rhee has reported that the tertiary allylic alcohol **9**, containing a carbocation-stabilizing phenyl group at the allylic position, converted quantitatively into 1-methoxy-5-phenyl-1,4-cycoheptadiene (**10**) using 2 mol % of $Ph_3PAuCl/AgSbF_6$.[12] The formation of **10** was suggested via a 5-*exo-dig* cyclization (to give **11**) followed by a [3,3]-sigmatropic rearrangement. The ionic intermediate **12**, however, would lead to six- or eight-membered carbocycles. Therefore, a concerted reaction pathway for rearrangement of **1a** is likely to proceed under the gold-catalyzed reaction conditions.



A reaction pathway was suggested in Scheme 2. Unlike addition of the olefin to the gold-activated alkyne in most

(10) (a) Toste, F. D.; Gorin, D. J. *Nature* **2007**, *446*, 395. (b) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (c) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402. (d) Yeh, M. C. P.; Tsao, W. C.; Lee, B. J.; Lin, T. L. *Organometallics* **2008**, *27*, 5326. For reviews on gold catalysts in organic synthesis, see: (e) Patil, N. T.; Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 3395.

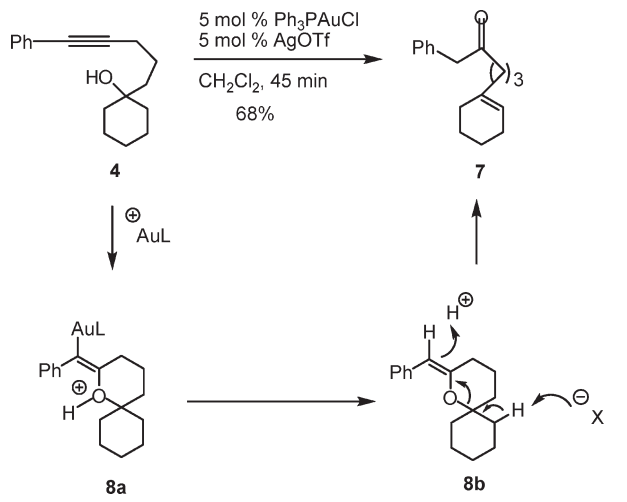
(11) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978.

(12) Bae, H. J.; Baskar, B.; An, S. E.; Cheong, J. Y.; Thangadurai, D. T.; Hwang, I. C.; Rhee, Y. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 2263.

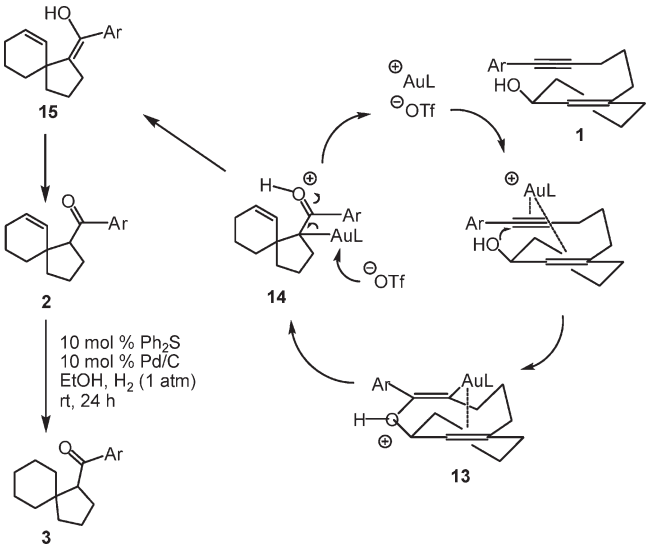
(13) Mori, A.; Miyakawa, Y.; Ohashi, E.; Haga, T.; Maegawa, T.; Sajiki, H. *Org. Lett.* **2006**, *8*, 3279.

(14) Jin, T.; Himuro, M.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 5893.

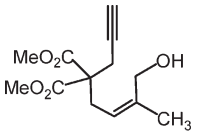
Scheme 1



Scheme 2



gold(I)-catalyzed cyclization of simple 1,6-enynes, a 9-*endo-dig* addition of the alcohol oxygen onto the gold-activated alkyne occurred. Coordination of the alkene to the gold center formed the cationic allylic vinyl gold intermediate **13**. In this way, it aligns two alkenyl moieties for further conversions. Moreover, the intermediate **13**, containing an oxonium ion, could greatly facilitate the key [3,3]-sigmatropic rearrangement. A similar allylic vinyl gold was suggested in the literature as a low-energy intermediate in the gold-catalyzed rearrangement of allenynes and N-allylic aminonitriles.[15] A subsequent Claisen-type rearrangement of the cyclic transient intermediate **13** produced the spirocyclic intermediate **14**, with a newly formed quarternary carbon center and a carbon−gold bond at the α-position of the carbonyl group. Attack of the triflate at the gold center of **14** furnished the spirocyclic enol **15** and release of the gold(I) catalyst into the catalytic cycle. Enol **15** led to spirocyclic ketone **2** as a 1:1 mixture of diastereomers. It is important to mention that an acyclic analogue of **1a**, for example the acyclic 2,7-enyn-1-ol **16**, underwent addition of alkene to the gold-activated alkyne in a 5-*exo-dig* fashion using 2 mol % of $Ph_3PAuCl/AgOTf$ to afford a gold cyclopropylcarbene followed by skeletal rearrangement to give 1,3-diene **17**.[16] In this case, the hydroxyl group did not participate as a competing nucleophile in the addition to the gold-activated terminal alkyne. Moreover, a gold(I)-catalyzed aza-Claisen-type rearrangement of pentenynyl allyl tosylamides to afford pyrroles only occurred with terminal alkynes,[17] and substrates bearing a phenyl group at the terminal position of the alkyne failed to generate the corresponding pyrrole using a high loading of the gold catalyst ($(pCF_3Ph)_3PAuNTf_2$). The failure of the cyclization may be due to an increased steric hindrance during the nucleophilic addition step of the tosylamide moiety onto the gold(I)-activated alkyne, while in the case of **1** the hydroxyl group added efficiently to the gold(I)-activated phenyl-substituted alkyne to generate the cationic allylic vinyl gold intermediate **13** (Scheme 2).



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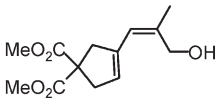

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Results of gold-catalyzed Claisen-type rearrangements of cyclic 8-aryl-2,7-enyn-1-ols **1a**−**e**, followed by olefin hydrogenation to produce spirocyclic ketones **3a**−**e**, are listed in Table 1. Electron-neutral and -rich arenes were proven to be good substrates, as the yields of desired spiroketones **3a**−**e** ranged from 60% to 85% in two steps (Table 1, entries 1−5). However, substrate **1f**, possessing a *para* bromine atom at the phenyl ring, was less effective and provided **2f** in 60% yield (Table 1, entry 6). To rule out the possibility of forming an allyl cationic intermediate catalyzed by gold(I) followed by attack of the pendant alkynyl group onto the allylic cation generating the spirocyclic ketones, the hydroxyl group was changed to the *O*-TBDMS (*tert*-butyldimethylsilyl) group, for example **1g** (Table 1, entry 7). The possible coordination of gold(I) to the oxygen atom should be prevented by the presence of the sterically demanding TBDMS group. The comparative isolated yields of **2a**, obtained from transformation of **1a** (90%) and the TBDMS ether **1g** (70%), respectively, may rule out the possible formation of highly reactive allyl cations and call for a coordination of the gold(I) to the pendant C−C triple bond, which is active during the ring-closing event (Scheme 2).[18] Moreover, the tertiary allylic alcohol with an ethyl group on the C-1 position, for example **1h**, also provided the spirocyclic ketone **2h** in 40% yield in 20 min under the standard reaction conditions (Table 1, entry 8). The low yield might be attributed to an increased steric hindrance during the nucleophilic addition step of the hydroxyl group onto the gold(I)-activated alkyne. This result may further indicate that the formation of a more stable tertiary carbocation by reaction of the gold(I) catalyst with **1h** did not occur. Therefore, these two examples

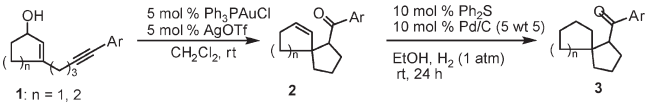
(15) (a) Heugebaert, T. S. A.; Stevens, C. V. *Org. Lett.* **2009**, *11*, 5018. (b) Lemiere, G.; Gandon, V.; Agenet, N.; Goddard, J.-P.; de Kozak, A.; Aubert, C.; Fensterbank, L.; Malacria, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 7596.

(16) (a) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (b) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Núñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem.—Eur. J.* **2006**, *12*, 1677.

(17) Istrate, F. M.; Gagosz, F. *Org. Lett.* **2007**, *9*, 3181.

(18) Bandini, M.; Eichholzer, A.; Kotrusz, P.; Tragni, M.; Troisi, S.; Umani-Ronchi, A. *Adv. Synth. Catal.* **2009**, *351*, 319.

Table 1. Gold(I)-Catalyzed Synthesis of Spiroketones 2 and Hydrogenation of 2 to Give Spiroketones 3



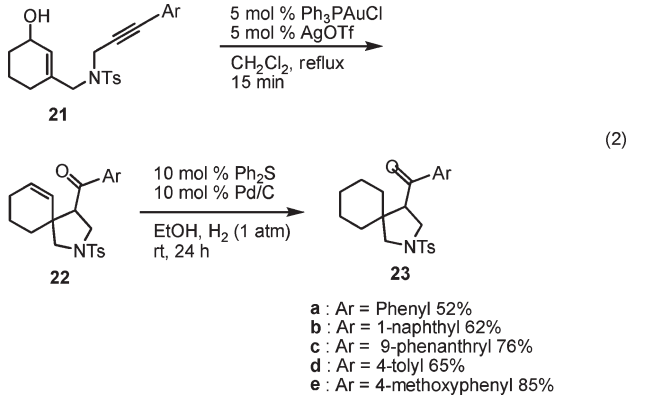
Entry	Substrate	time [min]	Product[a]	Yield [%]	Product	Yield[b] [%]
1	**1a** Ar = Ph	3	**2a**		**3a**	85
2	**1b** Ar = 1-naphthyl	3	**2b**		**3b**	60
3	**1c** Ar = 9-phenanthryl	3	**2c**		**3c**	82
4	**1d** Ar = 4-biphenyl	3	**2d**		**3d**	66
5	**1e** Ar = 4-methoxyphenyl	3	**2e**		**3e**	81
6	**1f** Ar = 4-bromophenyl	20	**2f**	60		
7	**1g**	30	**2a**		**3a**	66
8	**1h** Ar = 4-biphenyl	20	**2h**	40		
9	**18a** Ar = phenyl	3	**19a**		**20a**	77
10	**18b** Ar = 1-naphthyl	3	**19b**		**20b**	80
11	**18c** Ar = 4-biphenyl	3	**19c**		**20c**	64
12	**18d** Ar = 9-phenanthryl	3	**19d**		**20d**	76
13	**18e** Ar = 4-methoxyphenyl	3	**19e**		**20e**	76

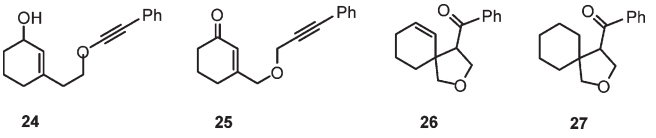
[a] All spiroketones **2a-h** and **19a-e** were isolated as a 1:1 mixture of two diastereomers.
[b] Yield of the isolated product in two steps.

(Table 1, entries 7, 8) may serve as mechanistic probes indicating a more concerted Claisen-type mechanism in the present case and exclude the possibility of the formation of allylic carbocationic intermediates. To further highlight the synthetic potential of the present catalytic cyclization, cyclic 2,7-enyn-1-ols with a methyl group or a hydrogen atom at the alkyne terminus were attempted. Unfortunately, both substrates failed to give the corresponding spirocycles even in the presence of 10 mol % of the catalyst, but instead resulted in the formation of unidentified products.

Five-membered-ring substrates **18a**−**e** also underwent Claisen-type rearrangement to provide spiro[4.4]nonenones **19a**−**e**, respectively, as a mixture of diastereomers in each case and in good yields (Table 1, entries 9−13). Upon use of 10 mol % Pd/C in the presence of Ph_2S, the hydrogenation of **19a**−**e** readily proceeded to give spirocyclic ketones **20a**−**e** in 64−80% yields in two steps.

The chemistry is general for the synthesis of nitrogen spirocycles. Substrates **21a**−**e**, containing an N-sulfonamide linkage in the tether, were prepared from treatment of 3-(bromomethyl)cyclohex-2-en-1-one with respective N-sulfonated arylpropagyl amines. In general, substrates **21a**−**e**, bearing an N-sulfonamide in the tether, reacted with the catalyst less efficiently at room temperature. Thus, the reaction was performed in refluxing CH_2Cl_2 for 15 min to give azaspirocycles **22a**−**e** as a 1:1 unseparable diastereomeric mixture (eq 2). These azaspirocycles were further hydrogenated (Pd/C/PhS_2/H_2) to give saturated azaspirocycles **23a**−**e** in 52−85% yields in two steps. Moreover, substrate **24**, containing two oxygen atoms at both allylic positions, was investigated. Compound **24** was prepared starting from addition of sodium hydride to the mixture of 3-(hydroxymethyl)cyclohex-2-en-1-one and 1-bromo-3-phenyl-2-propyne in tetrahydrofuran to give the enone **25**. Reduction of **25** with sodium borohydride in methanol afforded **24**. The cyclic enynol **24** was transformed into the expected oxaspirocyclic ketone **26** as a mixture of diastereomers in 62% yield using 5 mol % of the gold(I) catalyst in CH_2Cl_2 at 25 °C for 2 h. The oxaspirocycle **26** was selectively hydrogenated by the Wilkinson catalyst (10 mol % $Rh(PPh_3)_3Cl/H_2$) in ethanol at room temperature for 12 h to provide the oxaspirocycle **27** in 78% isolated yield. However, when treated with TfOH, compound **24** decomposed immediately. Therefore, the isolation of **26** may further provide evidence that the gold-catalyzed reaction did not proceed via an ionic pathway even when compound **24** contains a very sensitive allyl propagyl ether moiety.





We have described here a highly efficient gold(I)-catalyzed cycloisomerization of cyclic 8-aryl-2,7-enyn-1-ols featuring a Claisen-type rearrangement as the key step. The transformation is characterized by its efficiency, the mild conditions employed, and the easy formation of spiro[4.5]decane and spiro[4.4]nonane skeletons. This catalytic cyclization was applied to the formation of aza- and oxaspirocycles. The easy formation of spirocycles in an efficient way under mild reaction conditions may have further applications.

Experimental Section

General Considerations. All reactions were performed in oven-dried glassware under a nitrogen atmosphere unless otherwise indicated. Anhydrous solvents or reaction mixtures were transferred via an oven-dried syringe or cannula. Methylene chloride was predried by molecular sieves and then by passing through an Al_2O_3 column.[18] Flash column chromatography, following the method of Still, was carried out with E. Merck silica gel (Kieselgel 60, 230−400 mesh) using the indicated solvents.[19] ^1H nuclear

(19) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

magnetic resonance (NMR) spectra were obtained with Bruker-AC 400 (400 MHz) and 500 (500 MHz) spectrometers. The chemical shifts are reported in parts per million with either tetramethylsilane (0.00 ppm) or $CDCl_3$ (7.26 ppm) as internal standard. ^{13}C NMR spectra were recorded with Bruker-AC 400 (100 MHz) and 500 (125 MHz) spectrometers with $CDCl_3$ (77.0 ppm) as the internal standard. Infrared (IR) spectra were recorded with a JASCO IR-700 spectrometer. Mass spectra were acquired on a JEOL JMS-D 100 spectrometer at an ionization potential of 70 eV and were reported as mass/charge (*m*/*e*) with percent relative abundance. High-resolution mass spectra were obtained with an AEI MS-9 double-focusing mass spectrometer and a JEOL JMS-HX 110 spectrometer at the Department of Chemistry, Central Instrument Center, Taichung, Taiwan.

General Procedure for Gold(I)-Catalyzed Claisen-Type Rearrangement of Cyclic 8-Aryl-2,7-enyn-1-ols Followed by Hydrogenation. Synthesis of Spirocyclic Ketones 3. To an oven-dried 50 mL round-bottom flask equipped with a stirrer bar and capped with a rubber septum was added AgOTf (12 mg, 0.05 mmol). The apparatus was evacuated (oil pump) and filled with nitrogen three times. To the reaction mixture were then added via syringe 8-phenyl-2-cyclohex-1-ol (**1a**) (0.24 g, 1.0 mmol) and PPh_3AuCl (24 mg, 0.05 mmol) in 10 mL of CH_2Cl_2. The resulting mixture was stirred at room temperature for 3 min. The resulting dark blue solution was filtered through a bed of Celite. The filtrate was concentrated *in vacuo* to give the crude mixture. The residue was purified by flash column chromatography (silica gel, gradient elution: 5% to 10% ethyl acetate/hexanes) to give phenyl(spiro[4.5]dec-6-en-1-yl)methanone (**2a**) (0.22 g, 0.9 mmol, 90%) as a yellow oil. To an oven-dried 50 mL round-bottom flask equipped with a stirrer bar and capped with a rubber septum was added **2a** (0.22 g, 0.9 mmol) in 18 mL of ethanol at room temperature (ca. 30 °C) followed by addition of Pd/C (96 mg, 0.09 mmol) and diphenylsulfide (9 mg, 0.045 mmol). The air inside the reaction flask was evacuated and filled with a balloon of hydrogen twice. The reaction was vigorously stirred under 1 atm of hydrogen for 24 h. The crude mixture was filtered through a bed of Celite and eluted with dichloromethane (30 mL). The filtrate was concentrated to give the crude mixture.

Phenyl(spiro[4.5]decan-1-yl)methanone (3a). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **1a** (0.24 g, 1.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give **3a** (0.21 g, 0.85 mmol, 85%) as a yellow oil: IR (CH_2Cl_2) 2925, 2854, 1673, 1596, 1447, 1363, 1231, 1201 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.5 Hz, 2 H), 7.52 (t, J = 7.3 Hz, 1 H), 7.43 (t, J = 7.6 Hz, 2 H), 3.57 (t, J = 7.4 Hz, 1 H), 2.11 (m, 1 H), 1.89−1.82 (m, 2 H), 1.74 (m, 1 H), 1.70−1.62 (m, 2 H), 1.54−1.47 (m, 3 H), 1.41−1.37 (m, 4 H), 1.23 (m, 1 H), 1.07−0.98 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.8, 139.3, 132.6, 128.5, 128.4, 55.7, 48.0, 38.5, 35.7, 33.7, 28.8, 26.1, 23.8, 23.4, 23.2; MS (EI) *m*/*e* (%) 242.2 (M^+, 40), 146.1 (86), 145.1 (23), 133.1 (93), 122.2 (77) 120.1 (39), 105.1 (100), 81.1 (25), 77.1 (64), 55.1 (28); HRMS (EI) *m*/*e* calcd for $C_{17}H_{22}O$ 242.1672, found 242.1670.

Naphthalen-1-yl(spiro[4.5]decan-1-yl)methanone (3b). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **1b** (0.87 g, 3.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give naphthalen-1-yl(spiro[4.5]decan-1-yl)methanone **3b** (0.52 g, 1.8 mmol, 60%) as a yellow oil: IR (CH_2Cl_2) 2925, 2854, 1672, 1593, 1574, 1508, 1449, 1352, 1269, 1233, 1173 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 8.4 Hz, 1 H), 7.95 (d, J = 8.2 Hz, 1 H), 7.87 (d, J = 8.0 Hz, 1 H), 7.81 (d, J = 7.2 Hz, 1 H), 7.59−7.46 (m, 3 H), 3.58 (t, J = 7.7 Hz, 1 H), 2.25 (m, 1 H), 2.01−1.82 (m, 3 H), 1.70 (m, 1 H), 1.62−1.57 (m, 2 H), 1.46−1.23 (m, 8 H), 0.92 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1, 139.1, 134.3, 132.2, 130.2, 128.6, 127.8, 127.4, 126.5, 126.1, 124.5, 60.0, 48.9, 38.7, 36.1, 33.5, 28.6, 26.3, 23.8, 23.5, 23.0; MS (EI) *m*/*e* (%) 292.3 (M^+, 29), 196.1 (20), 183.1 (14), 170.1 (27), 156.1 (15), 155.1 (100), 127.1 (49); HRMS (EI) *m*/*e* calcd for $C_{21}H_{24}O$ 292.1819, found 292.1827.

Phenanthren-9-yl(spiro[4.5]decan-1-yl)methanone (3c). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **1c** (0.68 g, 2.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give **3c** (0.56 g, 1.64 mmol, 82%) as a yellow oil: IR (CH_2Cl_2) 2925, 2856, 1670, 1529, 1495, 1451 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 7.8 Hz, 1 H), 8.67 (d, J = 8.3 Hz, 1 H), 8.49 (d, J = 7.8 Hz, 1 H), 8.06 (s, 1 H), 7.95 (d, J = 7.8 Hz, 1 H), 7.74−7.60 (m, 4 H), 3.68 (t, J = 7.8 Hz, 1 H), 2.31 (m, 1 H), 2.02 (m, 1 H), 1.98−1.83 (m, 2 H), 1.73 (m, 1 H), 1.64−1.57 (m, 2 H), 1.46−1.23 (m, 8 H), 0.90 (m, 1 H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 207.69, 137.89, 131.62, 130.89 130.08, 129.68, 128.99, 128.48, 128.36, 127.26, 126.97, 126.78, 122.84, 122.62, 59.85, 48.76, 38.59, 35.88, 33.26, 28.36, 26.03, 23.65, 23.23, 22.76; MS (EI) *m*/*e* (rel intensity) 342.4 (M^+, 32), 220.2 (27), 206.2 (28), 205.2 (100), 177.1 (55), 176.1 (23); HRMS (EI) *m*/*e* calcd for $C_{25}H_{26}O$ 342.1989, found 342.1984.

Biphenyl-4-yl(spiro[4.5]decan-1-yl)methanone (3d). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **1d** (0.94 g, 3.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give **3d** (0.63 g, 0.19 mmol, 66%) as a yellow oil: IR (CH_2Cl_2) 3054, 2985, 2931, 2858, 2305, 1669, 1602, 1422, 1265 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02, (d, J = 8.3 Hz, 2 H), 7.68 (d, J = 8.3 Hz, 2 H), 7.64 (d, J = 7.4 Hz, 2 H), 7.47 (t, J = 7.5 Hz, 2 H), 7.39 (t, J = 7.3 Hz, 1 H), 3.61 (t, J = 7.4 Hz, 1 H), 2.13 (m, 1 H), 1.91−1.85 (m, 2 H), 1.76 (m, 1 H), 1.71−1.64 (m, 2 H), 1.58−1.50 (m, 3 H), 1.44−1.40 (m, 4 H), 1.28 (m, 1 H), 1.10−1.03 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.6, 145.4, 140.2, 138.1, 129.2, 129.1, 128.3, 127.5, 127.3, 56.0, 48.2, 38.8, 35.9, 33.9, 29.0, 26.3, 23.9, 23.5, 23.4; MS (EI) *m*/*e* (%) 318.3 (M^+, 34), 196.1 (86), 182.1 (15), 181.1 (100), 153.1 (24), 152.1 (41), 55.1 (19); HRMS (EI) *m*/*e* calcd for $C_{23}H_{26}O$ 318.1977, found 318.1984.

(4-Methoxyphenyl)(spiro[4.5]decan-1-yl)methanone (3e). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **1e** (0.81 g, 3.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give **3e** (0.66 g, 2.43 mmol, 81%) as a yellow oil: IR (CH_2Cl_2) 2934, 2856, 1664, 1600, 1576, 1508, 1450, 1418, 1364, 1306, 1261, 1236, 1170, 1112, 1031 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.8 Hz, 2 H), 6.93 (d, J = 8.8 Hz, 2 H), 3.85 (s, 3 H), 3.52 (t, J = 7.3 Hz, 1 H), 2.11 (m, 1 H), 1.88−1.79 (m, 2 H), 1.74 (m, 1 H), 1.69−1.63 (m, 2 H), 1.53−1.48 (m, 3 H), 1.43−1.37 (m, 4 H), 1.25 (m, 1 H), 1.05−0.99 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 163.3, 132.3, 130.7, 113.7, 55.5, 55.4, 47.9, 38.6, 35.7, 33.7, 28.8, 26.2, 23.8, 23.4, 23.3; MS (EI) *m*/*e* (%) 272.3 (M^+, 13), 176.1 (12), 163.1 (40), 135.1 (100), 107.1 (10), 92.1 (10), 77.1 (17), 55.1 (11); HRMS (EI) *m*/*e* calcd for $C_{18}H_{24}O_2$ 272.1770, found 272.1776.

(4-Bromophenyl)((1*S*,5*R*)-spiro[4.5]dec-6-en-1-yl)methanone (2f). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **1f** (0.95 g, 3.0 mmol) was purified by flash column chromatography (silica gel, gradient elution: 5% to 10% ethyl acetate/hexanes) to give **2f** (0.57 g, 1.80 mmol, 60%) as a yellow oil: dr = 1:1; IR (CH_2Cl_2) 2090, 1639, 1395, 1071, 1004 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.4 Hz, 2 H), 7.35 (d, J = 8.8 Hz, 2 H), 7.56 (d, J = 8.4 Hz, 4 H), 5.59−5.57 (m, 2 H), 5.48 (dt, J = 10.4, 3.6 Hz, 1 H), 5.36 (d, J = 10 Hz, 1 H), 3.64−3.57 (m, 2 H), 2.28−1.93 (m, 2 H), 1.93−1.39 (m, 22 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.89, 202.09, 137.63, 137.57, 135.69, 132.41, 131.60, 131.58, 130.09, 130.00, 127.70, 127.58, 126.95, 126.90, 55.79, 55.70, 48.50, 48.07, 41.89, 40.62, 35.92, 30.46, 29.70, 28.76, 28.56, 24.96, 24.85, 23.27,

22.99, 20.43, 20.18; MS (EI) *m*/*e* (%); HRMS (EI) *m*/*e* calcd for $C_{17}H_{19}BrO$ 318.0619, found 318.0623.

Biphenyl-4-yl(7-ethylspiro[4.5]dec-6-en-1-yl)methanone (2h). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **1h** (0.72 g, 2.0 mmol) was purified by flash column chromatography (silica gel, gradient elution: 5% to 10% ethyl acetate/hexanes) to give **2h** (0.13 g, 0.4 mmol, 40%) as a yellow oil: dr = 1:1; IR (CH_2Cl_2) 2961, 2093, 1664, 1187, 1005 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.4 Hz, 4 H), 7.92 (d, J = 8.4 Hz, 2 H), 7.63−7.57 (m, 12 H), 7.46 (t, J = 7.1 Hz, 6 H), 7.39 (d, J = 7.3 Hz, 3 H), 5.31 (s, 2 H), 4.99 (s, 1 H), 3.71 (t, J = 6.4 Hz, 1 H), 3.67 (t, J = 8.6 Hz, 3 H), 2.33−2.14 (m, 3 H), 1.8−1.6 (m, 38 H), 0.82 (t, J = 7.2 Hz, 6 H), 0.65 (t, J = 7.2 Hz, 3 H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.92, 202.97, 145.03, 144.82, 140.15, 140.12, 139.53, 139.38, 137.94, 137.84, 129.13, 129.03, 128.89, 128.73, 128.03, 127.24, 127.22, 126.80, 126.51, 125.71, 56.55, 55.93, 48.66, 48.26, 42.06, 40.48, 35.93, 30.51, 30.45, 30.21, 28.29, 28.14, 28.08, 28.04, 23.50, 22.82, 20.74, 20.56, 12.23, 12.06; MS (EI) *m*/*e* (%) 344 (M^+, 100), 209 (100), 181 (61), 136 (95), 110 (61); HRMS (EI) *m*/*e* calcd for $C_{25}H_{28}O$ 344.2140, found 344.2135.

5-Cyclohexenyl-1-phenylpentan-2-one (7). The crude mixture obtained from gold(I)-catalyzed rearrangement of **4** (0.17 g, 1.0 mmol) was purified by flash column chromatography (silica gel, gradient elution: hexanes to 2% ethyl acetate/hexanes) to give **7** (0.17 g, 0.07 mmol, 68%) as a colorless oil: IR (CH_2Cl_2) 2923, 2856, 1712, 1635, 1495, 1443, 1362 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34−7.30 (m, 2 H), 7.27−7.23 (m, 1 H), 7.21−7.18 (m, 2 H), 5.33−5.31 (m, 1 H), 3.67 (s, 2 H), 2.41 (t, J = 7.4 Hz, 2 H), 1.98−1.91 (m, 2 H), 1.90−1.81 (m, 3 H), 1.70−1.60 (m, 3 H), 1.60−1.55 (m, 2 H), 1.55−1.48 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.5, 136.84, 134.39, 129.38, 128.65 126.91, 121.66, 50.18, 41.29, 37.19, 27.97, 25.19, 22.91, 22.48, 21.56; MS (EI) *m*/*e* (%) 242.2 (M^+, 14), 151.1 (100), 133.1 (26), 108.2 (20), 67.1 (18).

Phenyl(spiro[4.4]nonan-1-yl)methanone (20a). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **18a** (0.45 g, 2.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give **20a** (0.35 g, 1.53 mmol, 77%) as a yellow oil: IR (CH_2Cl_2) 2863, 1676, 1445, 1361, 1224 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.2 Hz, 2 H), 7.54 (t, J = 7.2 Hz, 1 H), 7.45 (t, J = 7.2 Hz, 2 H), 3.73 (t, J = 6.8 Hz, 1 H), 2.19−2.08 (m, 1 H), 1.97−1.79 (m, 2 H), 1.77−1.66 (m, 2 H), 1.57−1.28 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.20, 138.90, 132.56, 128.49, 128.29, 55.53, 53.23, 39.66, 39.12, 34.15, 29.49, 24.29, 23.78, 22.22; MS (EI) *m*/*e* (%) 228.2 (M^+, 39), 146.1 (52), 133.1 (84), 108.1 (69), 106.1 (31), 105.0 (100), 81.1 (29), 77.0 (84), 67.0 (22); HRMS (EI) *m*/*e* calcd for $C_{16}H_{20}O$ 228.1507, found 228.1514.

Naphthalen-1-yl(spiro[4.4]nonan-1-yl)methanone (20b). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **18b** (0.55 g, 2.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give **20b** (0.45 g, 1.6 mmol, 80%) as a yellow oil: IR (CH_2Cl_2) 2944, 2875, 1673, 1595, 1573, 1511 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 8.6 Hz, 1 H), 7.94 (d, J = 8.2 Hz, 1 H), 7.86 (d, J = 7.9 Hz, 1 H), 7.78 (d, J = 7.16 Hz, 1 H), 7.58−7.45 (m, 3 H), 3.72 (dd, J = 7.5, 6.4 Hz, 1 H), 2.27−2.15 (m, 1 H), 2.05−1.96 (m, 1 H), 1.95−1.87 (m, 1 H), 1.85−1.77 (m, 1 H), 1.77−1.66 (m, 1 H), 1.59−1.39 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.25, 138.65, 134.02, 131.93, 130.04, 128.38, 127.54, 127.05, 126.29, 125.88, 124.26, 57.55, 55.93, 39.62, 39.15, 33.95, 29.19, 24.43, 23.68, 23.01; MS (EI) *m*/*e* (%) 278.2 (M^+, 54), 170.1 (41), 156.1 (23), 155.1 (100), 127.1 (67), 83.9 (21); HRMS (EI) *m*/*e* calcd for $C_{20}H_{22}O$ 278.1662, found 278.1670.

Biphenyl-4-yl(spiro[4.4]nonan-1-yl)methanone (20c). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **18c** (0.61 g, 2.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give **20c** (0.39 g, 1.28 mmol, 64%) as a yellow oil: IR (CH_2Cl_2) 2938, 2869, 1670, 1601, 1448, 1402 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 2 H), 7.69 (d, J = 8.3 Hz, 2 H), 7.65 (d, J = 7.3 Hz, 2 H), 7.48 (d, J = 7.2 Hz, 2 H), 7.41 (t, J = 7.3 Hz, 1 H), 3.77 (t, J = 7.8 Hz, 1 H), 2.16−2.05 (m, 1 H), 2.02−1.92 (m, 1 H), 1.91−1.85 (m, 1 H), 1.80−1.69 (m, 2 H), 1.62−1.54 (m, 6 H), 1.51−1.44 (m, 2 H), 1.43−1.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.74, 145.25, 139.96, 137.52, 128.92, 128.12, 127.25, 127.16, 55.60, 53.23, 39.70, 39.12, 34.19, 29.53, 24.31, 23.81, 23.26; MS (EI) *m*/*e* (%) 304.3 (M^+, 42), 209.1 (43), 196.1 (82), 181.1 (100), 153.1 (40), 152.1 (63); HRMS (EI) *m*/*e* calcd for $C_{22}H_{24}O$ 304.1825, found 304.1827. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2 and hexanes.

Phenanthren-9-yl(spiro[4.4]nonan-1-yl)methanone (20d). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **18d** (0.65 g, 2.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give **20d** (0.50 g, 1.51 mmol, 76%) as a yellow oil: IR (CH_2Cl_2) 2950, 2869, 1670, 1529, 1492, 1445 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 7.8 Hz, 1 H), 8.68 (d, J = 8.3 Hz, 1 H), 8.44 (d, J = 8.0 Hz, 1 H), 8.04 (s, 1 H), 7.93 (d, J = 11.4 Hz, 1 H), 7.75−7.61 (m, 4 H), 3.83 (dd, J = 7.7, 6.3 Hz, 1 H), 2.32−2.21 (m, 1 H), 2.11−2.01 (m, 1 H), 1.99−1.89 (m, 1 H), 1.88−1.72 (m, 2 H), 1.68−1.55 (m, 4 H), 1.54−1.45 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.08, 137.74, 131.60, 130.87, 130.08, 129.66, 128.84, 128.50, 128.42, 127.29, 127.00, 126.75, 122.84, 122.64, 57.57, 55.99, 39.65, 39.14, 33.96, 29.10, 24.51, 23.71, 22.98; MS (EI) *m*/*e* (%) 328.2 (M^+, 15), 311.2 (27), 205.1 (100), 191.1 (88), 177.1 (43); HRMS (EI) *m*/*e* calcd for $C_{24}H_{24}O$ 328.1820, found 328.1827.

(4-Methoxyphenyl)(spiro[4.4]nonan-1-yl)methanone (20e). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **18e** (0.51 g, 2.0 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 5% to 20% ethyl acetate/hexanes) to give **20e** (0.39 g, 1.51 mmol, 76%) as a yellow oil: IR (CH_2Cl_2) 2393, 2865, 1663, 1601, 1511, 1261, 1233, 1168, 1031 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.9 Hz, 2 H), 6.93 (d, J = 8.8 Hz, 2 H), 3.86 (s, 3 H), 3.67 (dd, J = 7.8, 6.3 Hz, 1 H), 2.15−2.03 (m, 1 H), 1.95−1.80 (m, 2 H), 1.78−1.67 (m, 2 H), 1.60−1.35 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.54, 163.13, 131.87, 130.52,113.59, 55.44, 55.37, 52.71, 39.63, 39.11, 34.07, 29.45, 24.23, 23.76, 23.22 ; MS (EI) *m*/*e* (%) 258.2 (M^+, 7), 163.1 (36), 150.1 (61), 135.0 (100); HRMS (EI) *m*/*e* calcd for $C_{17}H_{22}O_2$ 258.1624, found 258.1620.

Phenyl(2-tosyl-2-azaspiro[4.5]decan-4-yl)methanone (23a). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **21a** (0.12 g, 0.5 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 10% to 50% ethyl acetate/hexanes) to give **23a** (0.1 g, 0.25 mmol, 52%) as a yellow solid: mp 128−130 °C; IR (CH_2Cl_2) 2931, 1673, 1596, 1343, 1162 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.5 Hz, 2 H), 7.81 (d, J = 8.2 Hz, 2 H), 7.57 (t, J = 7.4 Hz, 1 H), 7.45 (t, J = 7.5 Hz, 2 H), 7.36 (d, J = 8.0 Hz, 2 H), 3.81 (t, J = 7.2 Hz, 1 H), 3.60 (dd, J = 10.0, 9.9 Hz, 2 H), 3.40 (d, J = 9.8 Hz, 1 H), 3.27 (d, J = 9.9 Hz, 1 H), 2.46 (s, 3 H), 1.62−1.51 (m, 3 H), 1.34−1.29 (m, 3 H), 1.09−0.90 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.43, 143.39, 137.96, 133.91, 133.39, 129.61, 128.71, 128.32, 127.55, 55.44, 53.34 49.19, 46.75, 36.49, 30.89, 25.41, 23.41, 22.97, 21.53; MS (EI) *m*/*e* (%) 397.2 (M^+, 0.1), 243.2 (17), 242.2 (100), 110.1 (23). 105.1 (57), 91.1 (25), 77.1 (18); HRMS (EI) *m*/*e* calcd for $C_{23}H_{27}NO_3S$ 397.1715, found 397.1711. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2 and hexanes.

Naphthalen-1-yl(2-tosyl-2-azaspiro[4.5]decan-4-yl)methanone (23b). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **21b** (0.22 g, 0.5 mmol) followed by

hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 10% to 50% ethyl acetate/hexanes) to give **23b** (0.14 g, 0.3 mmol, 62%) as a white solid: mp 165−167 °C; IR (CH_2Cl_2) 2913, 1673, 1597, 1340, 1162 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (m, 1 H), 7.99 (d, J = 8.2 Hz, 1 H), 7.83 (m, 1 H), 7.81 (d, J = 8.2 Hz, 2 H), 7.73 (d, J = 7.0 Hz, 1 H), 7.58−7.46 (m, 3 H), 7.38 (d, J = 8.1 Hz, 2 H), 3.83 (t, J = 7.3 Hz, 1 H), 3.71 (d, J = 7.4 Hz, 2 H), 3.42 (d, J = 9.9 Hz, 1 H), 3.34 (d, J = 9.9 Hz, 1 H), 2.47 (s, 3 H), 1.47−1.40 (m, 3 H), 1.33−1.02 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.89, 143.42, 136.93, 134.08, 133.06, 129.82, 129.66, 128.62, 128.06, 127.80, 127.62, 126.63, 125.42, 124.20, 56.96, 55.91, 48.94, 47.28, 36.49, 30.52, 25.44, 23.40, 22.95, 21.57; MS (EI) m/e (%) 447.3 (M^+, 0.4), 293.2 (20), 292.2 (100), 265.2 (16), 263.2 (19), 183.1 (12), 165.1 (11), 156.1 (13), 155.1 (99), 128.1 (11), 127.1 (63). 110.1 (26), 91.1 (34), 67.1 (11); HRMS (EI) m/e calcd for $C_{27}H_{29}NO_3S$ 447.1859, found 447.1860.

Phenanthren-9-yl(2-tosyl-2-azaspiro[4.5]decan-4-yl)methanone (23c). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **21c** (0.25 g, 0.5 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 10% to 50% ethyl acetate/hexanes) to give **23c** (0.18 g, 0.36 mmol, 76%) as a white solid: mp 187−189 °C; IR (CH_2Cl_2) 2931, 1731, 1668, 1598, 1338, 1161 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (dd, J = 19.0, 8.3 Hz, 2 H), 8.33 (d, J = 7.8 Hz, 1 H), 8.00 (s, 1 H), 7.93 (d, J = 7.8 Hz, 1 H), 7.83 (d, J = 8.0 Hz, 2 H), 7.74 (t, J = 7.8 Hz, 1 H), 7.69−7.58 (m, 3 H), 7.37 (d, J = 8.0 Hz, 2 H), 3.94 (t, J = 7.4 Hz, 1 H), 3.76 (t, J = 7.4 Hz, 2 H), 3.44 (d, J = 9.9 Hz, 1 H), 3.36 (d, J = 10.0 Hz, 1 H), 2.46 (s, 3 H), 1.49−1.06 (m, 9 H), 0.83 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.69, 143.40, 135.98, 134.01, 131.85, 130.88, 129.98, 129.84, 129.62, 129.11, 127.82, 127.55, 127.48, 127.26, 127.21, 126.24, 122.96, 122.64, 56.92, 55.84, 48.85, 47.32, 36.44, 30.50, 25.36, 23.34, 22.90, 21.51; MS (EI) m/e (%) 497.3 (M^+, 0.6), 343.3 (20), 342.3 (75), 313.2 (21), 265.2 (13), 233.2 (12), 232.1 (16). 215.1 (13), 206.1 (20), 205.1 (100), 191.1 (10). 178.1 (20), 177.1 (62), 176.1 (21), 110.1 (20), 91.1 (26), 67.1 (10); HRMS (EI) m/e calcd for $C_{31}H_{31}NO_3S$ 497.2030, found 497.2024.

***p*-Tolyl(2-tosyl-2-azaspiro[4.5]decan-4-yl)methanone (23d).** The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **21d** (0.2 g, 0.5 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 10% to 50% ethyl acetate/hexanes) to give **23d** (0.14 g, 0.33 mmol, 65%) as a white solid: mp 194−196 °C; IR (CH_2Cl_2) 2933, 1735, 1671, 1605, 1342, 1161 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.2 Hz, 2 H), 7.74 (d, J = 8.2 Hz, 2 H), 7.35 (d, J = 8.0 Hz, 2 H), 7.25 (d, J = 8.3 Hz, 2 H), 3.78 (t, J = 7.3 Hz, 1 H), 3.64−3.54 (m, 2 H), 3.40 (d, J = 9.8 Hz, 1 H), 3.25 (d, J = 9.8 Hz, 1 H), 2.46 (s, 3 H), 2.41 (s, 3 H), 1.64 (m, 1 H), 1.55−1.53 (m, 2 H), 1.36−1.26 (m, 3 H), 1.11−0.89 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.81, 144.28, 143.29, 135.45, 133.96, 129.54, 129.34, 128.43, 127.48, 55.41, 53.14, 49.18, 46.62, 36.43, 30.81, 25.38, 23.38, 22.93, 21.51, 21.46; MS (EI) m/e (%) 412.3 (M^+, 0.1), 257.2 (17), 256.2 (100), 147.1 (14), 119.1 (96), 110.1 (23). 91.1 (53), 65.1 (11); HRMS (FAB+) m/e calcd for $C_{24}H_{30}NO_3S$ 412.1952, found 412.1958. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2 and hexanes.

(4-Methoxyphenyl)(2-tosyl-2-azaspiro[4.5]decan-4-yl)methanone (23e). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **21e** (0.21 g, 0.5 mmol) followed by hydrogenation was purified by flash column chromatography (silica gel, gradient elution: 10% to 50% ethyl acetate/hexanes) to give **23e** (0.18 g, 0.42 mmol, 85%) as a white solid: mp 108−110 °C; IR (CH_2Cl_2) 1734, 1667, 1599, 1343, 1164 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.9 Hz, 2 H), 7.78 (d, J = 8.2 Hz, 2 H), 7.35 (d, J = 8.1 Hz, 2 H), 6.92 (d, J = 8.9 Hz, 2 H), 3.86 (s, 3 H), 3.76 (t, J = 7.3 Hz, 1 H), 3.60 (dd, J = 9.9, 9.8 Hz, 2 H), 3.39 (d, J = 9.85 Hz, 1 H), 3.26 (d, J = 9.85 Hz, 1 H), 2.45 (s, 3 H), 1.64−1.62 (m, 1 H), 1.55−1.53 (m, 2 H), 1.36−1.27 (m, 3 H), 1.1−0.87 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.48, 163.74, 143.29, 133.92, 130.88, 130.68, 129.54, 127.47, 113.81, 55.43, 52.92, 49.24, 46.57, 36.47, 30.79, 25.39, 23.41, 22.93, 21.46; MS (EI) m/e (%) 426.3 (M^+, 0.1), 273.2 (16), 272.2 (92), 163.1 (11), 136.1 (12), 135.1 (100), 110.1 (11). 91.1 (21); HRMS (EI) m/e calcd for $C_{24}H_{29}NO_4S$ 427.1816, found 427.1818.

Phenyl(2-oxaspiro[4.5]decan-4-yl)methanone (27). The crude mixture obtained from gold(I)-catalyzed Claisen-type rearrangement of **24** (0.12 g, 0.5 mmol) followed by hydrogenation with the Wilkinson catalyst[20] was purified by flash column chromatography (silica gel, gradient elution: 10% to 50% ethyl acetate/hexanes) to give **27** (0.059 g, 0.24 mmol, 48%) as a yellow liquid: mp 108−110 °C; IR (CH_2Cl_2) 1731, 1673, 1447, 1372, 1220 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.9 Hz, 2 H), 7.59 (m, 1 H), 7.51−7.4 (m, 2 H), 4.22 (dd, J = 8.4, 6.7 Hz, 1 H), 4.11 (dd, J = 8.2, 7.9 Hz, 1 H), 3.88−3.83 (m, 2 H), 3.76 (d, J = 8.5 Hz, 1 H), 1.79 (m, 1 H), 1.57−1.35 (m, 6 H), 1.17−1.06 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.67, 138.47, 133.15, 128.72, 128.38, 76.18, 70.46, 55.20, 48.63, 36.77, 31.20, 25.61, 23.87, 23.72; MS (EI) m/e (%) 244.2 (M^+, 14), 151.1 (10), 149.1 (51), 148.1 (14), 147.1 (30), 134.1 (12), 133.1 (74), 112.1 (27), 106.1 (11), 105.1 (100), 95.1 (13). 81.1 (14), 79.1 (13), 77.1 (62), 67.1 (17), 55.1 (22); HRMS (EI) m/e calcd for $C_{16}H_{20}O_2$ 244.1470, found 244.1463.

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra of compounds **2f**, **2h**, **3a**−**e**, **7**, **20a**−**e**, **23a**−**e**, and **27** and X-ray crystallographic information files for compounds **20c**, **23a**, and **23d**. This material is available free of charge via the Internet at http://pubs.acs.org.

(20) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.